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Effect of ICU care bundles on long-term patient-relevant outcomes: a scoping review

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ABSTRACT

Objective Care bundles are considered a key tool to improve bedside quality of care in the intensive care unit (ICU). We explored their effect on long-term patient-relevant outcomes.

Design Systematic literature search and scoping review.

Data sources We searched PubMed, Embase, CINAHL, APA PsycInfo, Web of Science, CDSR and CENTRAL for keywords of intensive care, care bundles, patient-relevant outcomes, and follow-up studies.

Eligibility criteria Original articles with patients admitted to adult ICUs assessing bundle implementations and measuring long-term (ie, ICU discharge or later) patient-relevant outcomes (ie, mortality, health-related quality of life (HrQoL), post-intensive care syndrome (PICS), care-related outcomes, adverse events, and social health).

Data extraction and synthesis After dual, independent, two-stage selection and charting, eligible records were critically appraised and assessed for bundle type, implementation strategies, and effects on long-term patient-relevant outcomes.

Results Of 2012 records, 38 met inclusion criteria; 55% (n=21) were before–after studies, 21% (n=8) observational cohort studies, 13% (n=5) randomised controlled trials, and 11% (n=4) had other designs. Bundles pertained to sepsis (n=11), neurocognition (n=6), communication (n=4), early rehabilitation (n=3), pharmacological discontinuation (n=3), ventilation (n=2) or combined bundles (n=9). Almost two-thirds of the studies reported on survival (n=24), 45% (n=17) on care-related outcomes (eg, discharge disposition), and 13% (n=5) of studies on HrQoL. Regarding PICS, 24% (n=9) assessed cognition, 13% (n=5) physical health, and 11% (n=4) mental health, up to 1 year after discharge. The effects of bundles on long-term patient-relevant outcomes was inconclusive, except for a positive effect of sepsis bundles on survival. The inconclusive effects may have been due to the high risk of bias in included studies and the variability in implementation strategies, instruments, and follow-up times.

Conclusions There is a need to explore the long-term effects of ICU bundles on HrQoL and PICS. Closing this knowledge gap appears vital to determine if there is long-term patient value of ICU bundles.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The protocol of this scoping review has been published in a peer-reviewed journal, and we followed the high standards of the Arksey and O'Malley framework and the Joanna Briggs Institute.
⇒ Our search strategy was independently peer-reviewed as recommended in the Peer Review of Electronic Search Strategies guidelines, and we conducted a comprehensive hand search of reference lists of all included studies and relevant reviews identified in the screening.
⇒ We grouped bundle implementation strategies using the *Expert Recommendations for Implementing Change* taxonomy of 73 implementation strategies.
⇒ Although not mandatory for scoping reviews, we conducted a quality appraisal of included studies using recommended tools from the Joanna Briggs Institute.
⇒ By using 'bundle' as an obligatory term in our search strategy, we may have missed articles that implemented bundle-like interventions without explicitly referring to them as 'bundles'.

INTRODUCTION

The complex environment of an intensive care unit (ICU) is characterised by severely ill patients[1] and a high density of treatment decisions.[2] On average, intensivists face more than 100 treatment decisions per day, where they put evidence-based measures into practice.[2] While intensive care research has focused on finding new therapies, little attention has been paid to knowledge transfer.[3] This led to a stark discrepancy between research-based best practice and bedside care.[3–7] For example, a study on the implementation of 11 evidence-based practices in the ICU found that best-practice care was prescribed in only 56.5% of the instances.[8] Existing ICU culture, low prioritisation on introducing novel care strategies, an ICU's organisational complexity, and lack of staff training have been identified as potential barriers to the implementation of evidence-based practices.[7]

Care bundles have been heralded as a potential remedy to leap the gap between evidence and practice.[9] Care bundles group three to five evidence-based practices.[10] Each bundle

element stands independently, is non-controversial, has a strong evidence base,[10] and the conjunctive application multiplies the effect on patient outcomes.[9] Each bundle element is clearly defined, and bundle implementation is monitored continuously.[10] Over the last decades, several ICU-specific bundles have emerged, such as the sepsis bundle of the Surviving Sepsis Campaign,[11] the ventilator bundle,[12] and the ABCDEF bundle.[13]

Bundle implementation studies in the ICU have commonly assessed bundle adherence,[14–17] ICU[14 17 18] or hospital mortality,[15 18] ICU length of stay,[17 18] costs,[17] and incidence of adverse events such as ventilator-associated pneumonia.[14 16] Undoubtedly, these short-term outcomes, which commonly focus on improvements in quality of care and clinical parameters, remain relevant. Yet, critical care research has acknowledged the importance of long-term patient-relevant sequelae of critical illness.[19–21] In addition to long-term mortality, these include a decreased health-related quality of life (HrQoL),[22] and specific morbidities like impairments of physical function,[23] cognition[24] and mental health,[25] summarised as post-intensive care syndrome (PICS).[26]

Previous reviews have explored the effect of non-pharmacological ICU interventions to improve long-term outcomes,[27] but we are unaware of previous research on ICU bundles. The effect of the implementation of ICU bundles on long-term patient-relevant outcomes appears unknown. First, we assessed if original ICU bundle research articles have reported effects on long-term patient-relevant outcomes. We included any study that assessed patient outcomes beyond ICU discharge. Second, we determined bundle types, implementation strategies, time points of outcome assessment of included studies. Given the heterogeneous nature of bundles, implementation strategies and outcomes, we considered a scoping review most suitable to answer the research question. With this work, we aim to identify knowledge gaps that may guide future studies on the long-term patient value of ICU bundles.

METHODS

Study design and definitions

We conducted a systematic literature search and scoping review to identify the effect of ICU bundles on long-term patient-relevant outcomes. We adhered to the Arksey and O'Malley framework[28] and additions,[29] and the Preferred Reporting Items for Systematic Review and Meta-Analysis Extension for Scoping-Reviews checklist (online supplemental file 1).[30] The scoping review was pre-registered on Open Science Framework,[31] and the protocol has been published.[32]

Patient-relevant outcomes were defined as outcomes of mortality, symptoms, adverse events/complications, and social health (eg, return to work).[33] Additionally, we included HrQoL and the PICS domains cognition, mental health and physical health. Long-term was defined as assessment at ICU discharge or later, except that we excluded mere assessment of hospital mortality.

Study identification

We searched PubMed, Embase (via Ovid), CINAHL and APA PsycInfo (via EBSCOhost), Web of Science, CDSR and CENTRAL on 12 December 2021 using a combination of English keywords and medical subject headings for four concepts: (1) intensive care, (2) care bundles, (3) patient-relevant outcomes, and (4) follow-up studies, without restrictions to the publication date (online supplemental table S1). On 21 August 2021, a preliminary search and independent pilot screening of 100 records by two authors (ERB and A-CK) was conducted to test and refine the search strategy, which adhered to the guidelines of Peer Review of Electronic Search Strategies (PRESS).[34]

Study selection

Search results were assessed in a two-stage process. Records were imported to EndNote (V.20.1, Clarivate Analytics, Philadelphia, USA) and, after duplicate removal, imported to Rayyan.[35] Two authors (NP and ERB) independently screened titles and abstracts using Rayyan's blinding option. Additionally, we conducted a hand search of reference lists of all included studies and relevant reviews identified in the screening to find additional literature. Two authors (NP and ERB) independently assessed the full texts of the remaining records. Disagreements between authors were solved through discussions. Reasons for exclusion were documented (online supplemental table S2).

Inclusion criteria were as follows: (1) participants were ≥18 years; (2) more than 50% of the patients received ICU treatment; (3) an ICU care bundle (≥3 bundled measures) was compared with standard care; (4) patient-relevant outcomes were measured at ICU discharge or later; (5) original research article; (6) published in English, German or Spanish. Exclusion criteria were as follows: (1) paediatric patients; (2) no measurement of patient-relevant outcomes at ICU discharge or later; (3) records were based on expert opinion or secondary research only.

Data charting and critical appraisal

Eligible records were charted individually by two authors (ERB and A-CK) using the Joanna Briggs Institute extraction form,[36] which was piloted with 10 publications and refined. Disagreements were resolved through discussions. Study designs were classified following the definitions of the Joanna Briggs Institute.[37] Experimental designs without randomised study arm allocation (eg, before–after designs) were classified as quasi-experimental studies. Studies that related the number of performed bundle items or bundle compliance to patient outcomes without implementing an intervention were classified as observational cohort studies. Bundles were categorised: (1) communication, (2) early

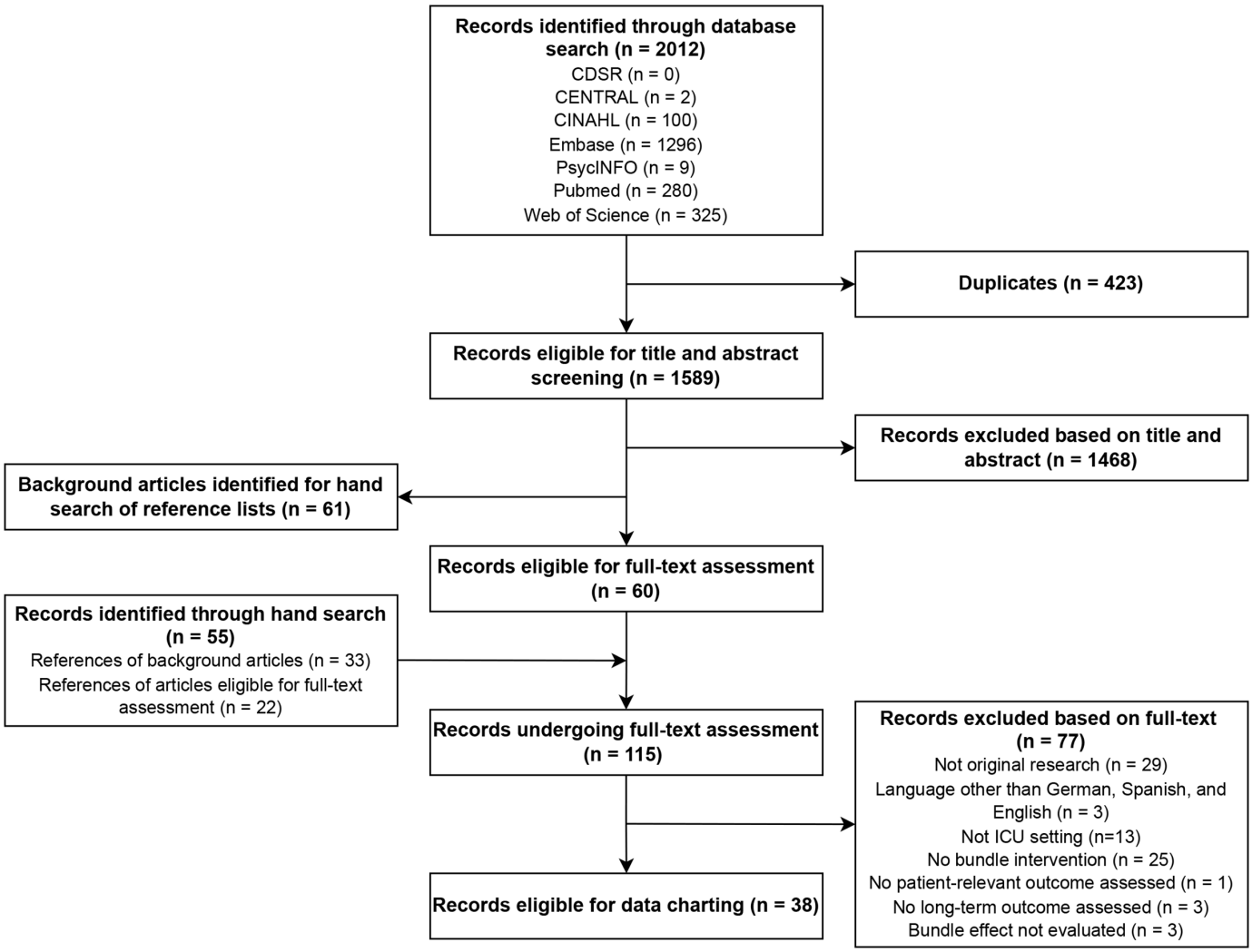

Figure 1 Study inclusion flowchart. ICU, intensive care unit.

rehabilitation, (3) neurocognition, (4) pharmacological discontinuation, (5) sepsis, (6) ventilation, and (7) combined bundles (eg, ABCDEF bundle). Outcomes were categorised: (1) survival, (2) HrQoL, (3) care-related outcomes (outcomes pertaining to care after discharge, ie, readmissions or discharge disposition), the PICS domains (4) cognition, (5) mental health, and (6) physical health/mobility, (7) social health (ie, return to work) and (8) adverse events. To enhance the comparability of implementation strategies, we adhered to the taxonomy of implementation strategies proposed in the *Expert Recommendations for Implementing Change (ERIC)* project.[38] Bundle effects of included studies on long-term patient-relevant outcomes were categorised as positive, possibly positive and no effect. Two authors (ERB and A-CK) individually performed a critical appraisal of included records using the Joanna Briggs Institute Critical Appraisal Tools.[37] Disagreements were resolved through discussions. Studies were not excluded based on inferior quality. Study data were managed using MS Excel (Microsoft Corporation, Redmond, Washington, USA).

Patient and public involvement

We did not involve patients in designing or conducting the review. For public involvement, we plan to disseminate our results through the authors' department website.

RESULTS

Characteristics of included studies

Of identified 2012 records, 60 remained for full-text assessment after dual title and abstract screening. We identified another 55 records through hand search of reference lists of background articles (n=33) and of articles included after screening (n=22). Of 115 records undergoing dual full-text assessment, 77 were excluded, leaving 38 records for dual charting (figure 1, online supplemental table S2).

Articles were published between 2000 and 2022, with half of the studies (n=19) published in 2016 or later. They were conducted in the US (n=15),[39–53] France (n=4),[54–57] Australia (n=5),[58–62] China (n=3),[63–65] Spain (n=2),[66 67] Norway (n=2),[68 69] Scotland,[70]

Portugal,[71] Northern Ireland,[72] Italy,[73] Germany,[74] Canada[75] and Uganda (each n=1).[76] Two studies depict separate outcome analyses of data collected within one clinical trial (ClinicalTrials.gov identifier: NCT01656317).[68 69] We identified 19 single-centre studies,[39–41 44 45 47 49 50 52 56 62–64 68 69 72–75] three two-centre studies,[43 57 76] and 16 multicentre studies.[42 46 48 51 53–55 58–61 65–67 70 71] Thirty studies were prospective,[39–45 48 51–59 61 62 64–69 71–73 75 76] and eight studies were retrospective.[46 47 49 50 60 63 70 74] Eight studies were observational cohort studies,[50 53 59 63 65 66 70 71] 21 studies were quasi-experimental before–after studies,[39–41 43–47 49 54–58 67–69 73–76] 1 study was a quasi-experimental single-arm study (which compared patients from the early and late implementation phases of a bundle intervention),[51] 1 study was a quasi-experimental controlled non-randomised comparative time-series study,[72] 1 study was a cost-effectiveness analysis,[42] 5 studies were randomised controlled trials (RCTs) (one cluster RCT and 4 individually RCTs)[48 52 61 62 64] and 1 study was a quasi-experimental trial following an RCT.[60] Settings varied from 42 hospitals[59] and 68 ICUs[53] to 1 ICU.[50 75] Sample sizes varied from 36 055[70] to 30[62] (online supplemental table S3).

Bundle type and implementation strategies

Eleven studies investigated the implementation of a sepsis bundle based on recommendations from the Surviving Sepsis Campaign or similar.[44 45 54 63–67 71 74 76] Nine studies explored combined bundles, including five studies on the ABCDE(F) bundle,[41–43 53 62] one study on geriatric-focused practices,[50] two studies on a fever, sugar and swallowing bundle[60 61] and one study comprising delirium and sedation management, mobilisation and rounding strategies.[46] Six studies explored the implementation of neurocognitive bundles, with one sleep quality intervention,[40] one psychological intervention,[73] two stroke bundles,[59 70] one cognitive and physical therapy bundle,[52] and one bundle on protocolised sedation, analgesia and delirium management.[75] Four studies investigated the implementation of a communication bundle, which comprised interaction with patient and family.[39 47 51 72] Three bundles pertained to early rehabilitation.[56 68 69] Three studies investigated pharmacological discontinuation bundles on stress ulcer prophylaxis discontinuation,[58] antipsychotic medication discontinuation[49] and pharmacological delirium management.[49] Two studies were about ventilation bundles with lung-protective ventilation and early extubation[55 57] (table 1, online supplemental table S3).

We identified 44 *ERIC* implementation strategies to implement bundles. Most commonly, studies conducted educational meetings (n=23) such as seminars or supervised training, or developed and implemented tools for quality monitoring (n=19), for example, change cycles and algorithms. Often studies developed (n=13) and distributed (n=12) educational materials by, for example, uploading information to the institute's website or providing posters. Studies identified and prepared

Table 1 Categories of long-term patient-relevant outcomes, by bundle category

Outcome and bundle category	All (n=38)	Combined bundle (n=9)*	Communication (n=4)	Early rehabilitation (n=3)	Neurocognition (n=6)	Pharmacological discontinuation (n=3)	Sepsis (n=11)	Ventilation (n=2)
Survival	24 (63)	4 (44)	1 (25)	3 (100)	3 (50)	1 (33)	11 (100)	1 (50)
Care-related outcome†	17 (45)	6 (67)	3 (75)		3 (50)	2 (67)	1 (9)	2 (100)
Health-related quality of life	5 (13)	2 (22)			3 (50)			
PICS—physical health	5 (13)	2 (22)		2 (67)	1 (17)			
PICS—cognition	9 (24)	2 (22)		3 (100)	3 (50)			1 (50)
PICS—mental health	4 (11)	1 (11)	1 (25)		1 (17)	1 (33)		
Social health	1 (3)				1 (17)			
Adverse events	1 (3)			1 (33)				

n (%).
*Includes the ABCDEF bundle.
†Care-related outcomes comprise outcomes pertaining to care after intensive care unit discharge, eg, readmissions or discharge disposition.
PICS, post-intensive care syndrome.

champions (n=11) to implement the intervention in their ICU and built a coalition to strengthen partner relationships (n=10). Studies rarely involved executive boards or used advisory boards and workgroups. Notably, reporting of implementation strategies was not standardised, and four studies did not report any implementation strategy (table 2).

Long-term patient-relevant outcomes used

Almost two-thirds (n=24) of the studies reported survival after hospital discharge, most commonly 28-day,[44–46 54 63–67 71 76] 30-day,[48 70 74 75] 60-day,[63] 90-day,[57 61 63 69] 180-day,[59 70] 1 year,[42 56 68] or 3–5 year mortality,[60] or survival to discharge from acute and rehabilitative care to home and mortality in the rehabilitation facility[39] (tables 1 and 3).

Long-term HrQoL was assessed in five studies.[42 52 59 62 73] Concerning the PICS domains, nine studies assessed cognition,[40 52 55 56 61 62 68 69 73] five studies assessed physical health,[52 56 61 62 69] and four studies assessed mental health.[49 61 72 73] Care-related outcomes, that is, outcomes associated with patient care after discharge, were assessed in 17 studies. These include discharge destination,[42 47 48 50 51 53 59] change in residence,[41 70] return to independent living,[75] hospital or ICU readmission rates,[43 53] inappropriate continuation of stress ulcer prophylaxis at discharge,[58] ICU-free days and ventilator-free days,[55 57 74] risk of remaining in the ICU[39] or discharge diagnosis of aspiration pneumonia.[61] One study assessed adverse events within 90 days after stroke,[69] and one study assessed return to work within 12 months[73] (tables 1 and 3). Notably, even within similar outcome categories (eg, mental health), studies varied with respect to test instruments used. Further, the time points of outcome measurement varied from ICU discharge to 3–5 years after stroke onset[60] (table 3).

Effects on long-term patient-relevant outcomes

We grouped studies based on the effect on patient-relevant outcomes, but due to the variability in instruments and time points, we did not perform a meta-analysis. Thirteen studies found a positive effect of the bundle intervention on survival,[44 45 54 55 59 64–67 70 71 74 76] whereas nine studies did not find a survival benefit.[39 46 48 56 57 63 68 69 75] Interestingly, 10 of 11 studies on sepsis bundles showed superior survival. For care-related outcomes, HrQoL, and the PICS domains cognition, mental health and physical health, we found mixed evidence: Some studies detected a positive effect, others possibly a positive effect, and other studies could not find any effect at all (table 4, online supplemental table S4).

As an example of a positive effect on PICS outcomes, a before–after study in an Italian mixed ICU evaluated an in-ICU psychological intervention including emotional support to patients and family members, counselling, stress management, coping strategies and family-centred decision-making. One year after ICU discharge, fewer patients from the intervention group showed a high risk for post-traumatic stress disorder (21.1% vs 57%) or needed psychiatric medication after discharge (1.7% vs 8.1%), and their HrQoL was higher (EQ-5D visual analogue scale 77.4 vs 72.4). No significant differences were found concerning anxiety, depression, and return to previous employment.[73]

Critical appraisal

In almost half of the RCTs and the quasi-experimental studies (n=12/30), baseline characteristics of control and intervention group significantly differed, posing a high risk of confounding bias.[40–42 45 52 54 57 58 62 74–76] The proportion of studies lacking comparability of study groups could be even higher as articles frequently lacked information to assess the comparability of the study groups. Another issue with included RCTs was the lack of blinding: All RCTs (n=5) blinded the outcome assessor for treatment assignment, but only one study reported patient blinding,[61] and no study reported study team blinding. The reliability of outcome measures in quasi-experimental studies was often compromised or not reported. In three studies, participants selectively received different care other than the exposure, making these studies prone to confounding bias.[46 57 69] In two of eight cohort studies, the study groups did not originate from the same population, posing a risk of selection bias[59 66] (online supplemental tables S5–S7).

DISCUSSION

Main findings

We conducted a scoping review on the long-term effects of ICU bundles on patient-relevant outcomes. Our five main findings were as follows: First, most included studies reported long-term survival or care-related outcomes, but few studies assessed HrQoL or PICS-related outcomes of cognition, mental health and physical health. Second, even if studies assessed HrQoL or PICS, we found little standardisation in methodology, instruments and follow-up time. Third, most studies on sepsis bundles found a positive effect on survival, but there was no conclusive positive effect of other bundles on different patient-relevant outcome categories. Fourth, interventions commonly relied on simple implementation strategies such as conducting educational meetings. Fifth, while studies were conducted in a variety of settings, more than half were before–after studies and half were single-centre studies. In the critical appraisal, we identified a high risk of bias.

What is already known

Outside of ICU bundle implementation research, the epidemiology of long-term sequelae after critical illness is well described: Up to 34% of the patients show anxiety symptoms 12–14 months after ICU discharge,[77] up to 29–30% have depressive symptoms 12–14 months after discharge,[78] and up to 34% have symptoms of post-traumatic stress disorder.[79] Cognitive impairments occur in 4–62% of the patients,[80] 5–70% show dependencies in

Table 2 Implementation strategies* used in included studies (n=38), in descending order

Implementation strategy	n (%)	References
Conduct educational meetings	23 (61)	40–47 49 51 54–58 60–62 67 71–73 75
Develop and implement tools for quality monitoring	19 (50)	40 43–47 49 51 52 54–57 62 67 68 71 75 76
Develop educational materials	13 (34)	41 47 49 51 54–56 58 60 61 67 71 72
Distribute educational materials	12 (32)	41 47 49 51 54–56 58 60 61 71 72
Identify and prepare champions	11 (29)	40–43 48 51 60 61 71 75 76
Build a coalition	10 (26)	40 41 43 47 49 51 52 68 71 75
Audit and provide feedback	9 (24)	39 41–43 46 51 60 61 67
Conduct ongoing training	8 (21)	41 43 45 47 49 51 56 75
Develop and organise quality monitoring systems	8 (21)	41 42 46–48 51 65 71
Develop a formal implementation blueprint	7 (18)	41 43 47 51 54 65 71
Provide ongoing consultation	6 (16)	43 48 60–62 71
Change record systems	5 (13)	41–43 46 71
Stage implementation scale up	5 (13)	40 46 47 62 72
Create new clinical teams	5 (13)	41 43 47 60 61
Involve patients/consumers and family members	4 (11)	39 47 72 76
Centralise technical assistance	4 (11)	46 48 62 71
Assess for readiness and identify barriers and facilitators	4 (11)	43 49 60 61
Remind clinicians	4 (11)	40 48 60 61
No strategy reported	4 (11)	51 61 63 70
Conduct educational outreach visits	3 (8)	51 60 61
Tailor strategies	3 (8)	47 49 75
Provide clinical supervision	3 (8)	43 48 73
Purposely re-examine the implementation	3 (8)	41 54 57
Conduct local consensus discussions	2 (5)	41 75
Organise clinician implementation team meetings	2 (5)	41 55
Facilitation	2 (5)	43 72
Provide local technical assistance	2 (5)	48 71
Change physical structure and equipment	2 (5)	40 75
Conduct cyclical small tests of change	2 (5)	46 47
Mandate change	2 (5)	43 47
Develop academic partnerships	2 (5)	43 71
Make training dynamic	2 (5)	55 62
Create a learning collaborative	1 (3)	41
Recruit, designate, and train for leadership	1 (3)	41
Intervene with patients/consumers to enhance uptake and adherence	1 (3)	72
Obtain and use patients/consumers and family feedback	1 (3)	72
Prepare patients/consumers to be active participants	1 (3)	72
Facilitate relay of clinical data to providers	1 (3)	68
Conduct local needs assessment	1 (3)	65
Inform local opinion leaders	1 (3)	46
Use an implementation advisor	1 (3)	46
Involve executive boards	1 (3)	43
Work with educational institutions	1 (3)	43

Continued

Table 2 Continued

Implementation strategy	n (%)	References
Promote adaptability	1 (3)	75
Use advisory boards and workgroups	1 (3)	75

Studies[68 69] are separate outcome analyses of unique data collected within one clinical trial (ClinicalTrials.gov identifier: NCT01656317).
*According to the *Expert Recommendations for Implementing Change (ERIC)* taxonomy.[38]

instrumental activities of daily living,[81] and the HrQoL is below population norms.[22]

Although the high frequency of long-term impairments constitutes an imperative to include these outcomes in ICU bundle research, no other review of ICU bundles has focused on long-term patient-relevant outcomes. Previous reviews have assessed ICU bundle implementation strategies,[82] barriers and facilitators of ICU bundle implementation[83] and the effect on outcomes.[84] Our results support previous reviews, which concluded that studies implementing ICU bundles often lack structure regarding use, reporting and justification of implementation strategies.[83 84] In line with previous reviews,[82–84] we showed that some implementation strategies (eg, educational activities and audit and feedback) were more frequently used than others. We translated implementation strategies to the respective *ERIC* strategies to enhance comparability; however, just like previous reviews on ICU bundles found out,[83] none of our included studies used the *ERIC* taxonomy. Another scoping review for evidence-based practices in critical care in general also found considerable variability in the nomenclature that was used to describe implementation strategies.[85] Standardised and transparent reporting is recommended to compare the effectiveness of certain strategies.[83 86] Corresponding to our critical appraisal, previous reviews also found that most evidence on ICU bundle effects has weak methodological quality.[85] In our work, half of the studies were conducted in a single centre, making them prone to centre-specific effects such as local ICU culture. Unknown centre-specific effects may limit the generalisability of results to other hospitals and contexts.

Practical implications and directions of future research

Our work yields practical implications and directions for future research. Studies on ICU bundles that used long-term patient-relevant outcomes mostly assessed mortality or care-related outcomes, but HrQoL and PICS appear rarely assessed. Hence, this scoping review identified a research gap for high-quality research on the effect of ICU bundles on HrQoL and PICS, but not so much on mortality and care-related outcomes. Closing the research gap is difficult as post-ICU follow-up studies take time and are challenging for research teams.[87] Reasons include high post-ICU mortality, loss to follow-up, missing data, instrument selection and high demands on constraint time and personnel.[87] However, the relevance for patients provides a strong impetus for conducting these studies, with observation periods ideally years after discharge. To ease the comparison and facilitate results synthesis in meta-analyses, there is a need to adhere to a common and standardised instrument set (eg,[88 89]). The definition of a core outcome set for long-term effects of ICU bundle interventions, which could be included in the Core Outcome Measures in Effectiveness Trials initiative database,[90] may facilitate the harmonisation.

We identified several studies that implemented a sepsis bundle and found a positive effect on long-term survival. Hence, as a practical implication, clinicians may consider using multicomponent implementation strategies to implement a sepsis bundle, ideally using a theory-guided approach.[91] For a stronger recommendation, studies identified in this review could be included in a meta-analysis. For other bundles, for example, neurocognitive bundles or combined bundles (including the ABCDEF bundle), we found little and inconclusive evidence of improved outcomes. Hence, at this point we are unable to recommend that intensivists implement these bundles to improve long-term patient-relevant outcomes. The variation in instruments and time points, the risk of bias and the varying complexity level of implementation strategies may have contributed to the unequivocal conclusions on the bundle effects. ICU bundles may improve short-term patient outcomes, but the low-quality evidence has already prevented a clear recommendation for ICU bundle implementation in a previous review.[84]

Strengths and limitations

Strengths of this scoping review include the rigorous methodology: First, the review was preregistered on Open Science Framework[31] and its protocol was published.[32] Second, the search strategy was developed according to PRESS recommendations.[34] Third, we performed an extensive hand search to collect records missed by our search strategy. Fourth, selection, charting and critical appraisal were performed independently by two researchers. Fifth, though not mandatory for scoping reviews, we performed a quality appraisal. Finally, we used the *ERIC* framework to group implementation strategies,[38] which enhances the comparability to other studies.

Limitations of this work also warrant consideration. First, there is no consensus on a definition of patient-relevant outcomes. We intended to use a broad definition that included general and ICU-specific outcomes but might have missed relevant studies. Second, there is no consensus on the definition of long-term. We used a broad definition of ICU discharge or later to include any study that assessed outcomes beyond a patient's ICU

Table 3 Instruments and evaluation periods for the assessment of long-term patient-relevant outcomes

Outcome category	Instruments	At discharge*	After discharge*						Other time	References
			28–30 d/1 m	60 d/2 m	90 d/3 m	180 d/6 m	1y	3–5 y		
Survival (n=24)	Mortality		x†							44–46 48 54 64–67 71 74–76
			x	x	x					63
					x					57 61 69
					x‡					61 69
			x‡			x‡				70
						x‡				59
							x§			42
							x¶			42 56 68
								x‡		60
									At discharge to rehabilitation, to home and in rehabilitation	39
HrQoL (n=5)	SF-36				x					62
	EQ5D VAS				x					52
	EQ5D VAS				x**	x**				59
	EQ5D domain scores, EQ5D VAS						x			73
	QALYs						x§			42
PICS—cognition (n=9)	Modified Rankin Scale; Glasgow Outcome Scale Extended						x¶			68
	Glasgow Outcome Scale				x¶					55
	Modified Rankin Scale				x§					61
	Functional Independence Measure	x								62
	CAM-ICU; Digit Span Forward and Backward test; TMT A and B	x††								40
	Tower Test; dysexecutive questionnaire, MMSE	x			x					52
	Glasgow Coma Scale	x								69 73
	ASIA motor and sensitive score	x					x¶			56
PICS—physical health (n=5)	Physical Function ICU Test-scored, Functional Independence Measure	x								62
	Timed Up-and-Go; Katz Activities of Daily Living; Functional Activities Questionnaire	x			x					52
	Mobilisation level	x								69
	ASIA motor and sensitive score	x					x¶			56
	Mean physical component summary score, Barthel index				x§					61

Continued

Table 3 Continued

Outcome category	Instruments	At discharge*	After discharge*						Other time	References
			28–30 d/1 m	60 d/2 m	90 d/3 m	180 d/6 m	1y	3–5 y		
PICS—mental health (n=4)	Sickness Impact Profile		x§	x§	x§					72
	IES-R; HADS; need for psychotherapy, anxiolytic and/or antidepressant medication						x			73
	Antipsychotic medication use	x								49
	Mean SF-36 mental component summary score				x§					61
Care-related outcomes (n=17)	Discharge destination	x								42 47 48 50 51 53 59
	Change in residence	x								41
	Discharge to usual residence		x§			x§				70
	Return to independent living	x								75
	ICU readmission rate, ICU discharge destination other than home	x								53
	Inappropriate continuation of stress ulcer prophylaxis	x								58
	ICU-free days and ventilator-free days				x¶					55 57
	Ventilator-free days		x‡‡							57 74
	Readmission rate		x							43
	Risk of remaining in the ICU								Until day 20	39
	Discharge diagnosis of aspiration pneumonia	x								61
Adverse events (n=1)	Adverse events				x‡					69
Social health (n=1)	Return to work						x			73

Studies[68 69] are separate outcome analyses of unique data collected within one clinical trial (ClinicalTrials.gov identifier: NCT01656317).
*ICU and/or hospital discharge.
†After discharge, except for one study that considered those discharged before 28 days to be alive[44] and one study that assessed 30-day mortality after hospital admission.[76]
‡After stroke.
§After ICU/hospital admission.
¶After trauma/haemorrhage.
**EQ5D VAS measured at 90-180 days after the index event.
††Right after ICU discharge.
‡‡After trauma[57] or hospital admission.[74]
ASIA, American Spinal Injury Association; CAM-ICU, Confusion Assessment Method for the ICU; d, days; EQ5D, EuroQol 5 dimensions; HADS, Hospital Anxiety and Depression Scale; HrQoL, health-related quality of life; ICU, intensive care unit; IES-R, Impact of Event Scale-Revised; m, months; MMSE, Mini-Mental State Examination; QALY, quality-adjusted life year; SF-36, Short Form (36); TMT, Trail Making Test; VAS, visual analogue scale; y, years.

Table 4 Effects of bundles on long-term patient-relevant outcomes

Bundle category	Outcome	Effect		
		Positive	Possibly positive	None
All (n=38)	Survival	13[44 45 54 55 59 64–67 70 71 74 76]	2[60 61]	9[39 46 48 56 57 63 68 69 75]
	Care-related outcomes *	12[39 42 49–51 53 55 57–59 70 75]	4[43 47 61 62]	5[41 48 69 73 74]
	Health-related quality of life	2[59 73]	2[42 62]	1[52]
	PICS—physical health	3[56 61 69]		2[52 68]
	PICS—cognition	1[56]		3[40 52 68]
	PICS—mental health	2[72 73]		1[61]
	Adverse events			1[69]
	Social health			1[73]
Communication (n=4)	Survival			1[39]
	Care-related outcomes*	2[39 51]	1[47]	
	PICS—mental health	1[72]		
Early rehabilitation (n=3)	Survival			3[56 68 69]
	Care-related outcomes*			1[69]
	PICS—physical health	2[56 69]		1[68]
	PICS—cognition	1[56]		1[68]
	Adverse events			1[69]
Neurocognitive (n=6)	Survival	2[59 70]		1[75]
	Care-related outcomes*	3[59 70 75]		1[73]
	Health-related quality of life	2[59 73]		1[52]
	PICS—physical health			1[52]
	PICS—cognition			2[40 52]
	PICS—mental health	1[73]		
	Social health			1[73]
Pharmacological discontinuation (n=3)	Survival			1[48]
	Care-related outcomes*	2[49 58]		1[48]
Sepsis (n=11)	Survival	10[44 45 54 64–67 71 74 76]		1[63]
	Care-related outcomes*			1[74]
Ventilation (n=2)	Survival	1[55]		1[57]
	Care-related outcomes*	2[55 57]		
Combined (n=9)†	Survival	1[42]	2[60 61]	1[46]
	Care-related outcomes*	3[42 50 53]	3[43 61 62]	1[41]
	Health-related quality of life		2[42 62]	
	PICS—physical health	1[61]		
	PICS—mental health			1[61]

Studies[68 69] are separate outcome analyses of unique data collected within one clinical trial (ClinicalTrials.gov identifier: NCT01656317).
*Care-related outcomes comprise outcomes pertaining to care after ICU discharge, eg, readmissions or discharge disposition.
†Includes the ABCDEF bundle.
ICU, intensive care unit; PICS, post-intensive care syndrome.

stay, but our pragmatic definition resulted in the inclusion of studies that only measured outcomes shortly after or at ICU discharge. A more restrictive definition would have drastically reduced the number of included studies. Third, by including 'bundle' as a necessary term in our search strategy, we may have missed articles that described multicomponent interventions without referring to them as bundles. For example, a recently published cluster RCT evaluated the effects of an individually tailored, multicomponent nursing intervention on delirium prevention, which may be considered a bundle. Despite implementation efforts, the time spent on intervention components, ICU readmission rate, 28-day and 90-day mortality did not improve significantly.[92] The term 'bundle' has been well-established for many years, and we mitigated the risk of missing relevant articles by conducting a comprehensive hand search. Fourth, the research question and search strategy were developed by a research team with expertise in critical care, quality improvement, care bundles, PICS and post-ICU follow-ups. While this expertise relates

to many areas of the review, the clinical focus may have biased our results. Finally, as this was not intended in our study protocol,[32] we did not synthesise the effects of the included studies. A synthesis could be performed in future meta-analyses, despite the challenges due to the heterogeneity of implemented bundles, outcomes, instruments and time points.

CONCLUSIONS

Our systematic literature search and scoping review identified 38 studies on the effect of ICU bundles on long-term patient-relevant outcomes. The studies pertained to a variety of bundles, most commonly the sepsis bundle. The majority were quasi-experimental before–after studies and single-centre or two-centre studies with bias risks identified in the critical appraisal. Despite their undisputed relevance for patients, we only identified a few studies that reported long-term HrQoL and PICS outcomes of cognition, mental health and physical health. While most studies on sepsis bundles indicated a survival benefit, the effect of other bundles on different long-term patient-relevant outcomes was inconclusive. This may have been due to the large variability in instruments and time points. Hence, future research should focus on: (1) Assessing long-term HrQoL and PICS-related outcomes; (2) using standardised instruments and common time points; (3) employing high-quality research designs and clearly describing bundle interventions and implementation strategies.

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